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The Risk of Diagnosed Fractures in Children with Inflammatory Bowel Diseases

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Abstract

Background & Aims—Decreased bone mass is common in children with inflammatory bowel diseases (IBD); however, fracture risk is unknown. We sought to evaluate fracture risk in children with IBD as compared to unaffected controls and determine whether this risk is affected by geographical region (a proxy for sun/vitamin D exposure) and oral steroid use.

Methods—We identified cases of Crohn's disease (CD) and ulcerative colitis (UC), less than 20 years of age, using administrative data from 87 health plans. Each case was matched to 3 controls, on the basis of age, gender, and geographical region. We identified fractures in cases and controls using ICD-9 diagnosis codes, and measured oral steroid exposure using NDC codes.

Results—The study included 733 children with CD, 488 with UC, and 3287 controls (mean age 15 years). IBD was not associated with a higher risk of fracture at any site [CD OR 0.8 (95% CI 0.6-1.1; UC OR 1.4 (95% CI 1.0-2.1)] or at multiple sites [CD OR 0.8 (95% CI 0.4-1.7; UC OR 0.4 (95% CI 0.1-1.4)]. Among IBD patients, we did not identify any significant differences in the fracture rate between those residing in the Northeast/Midwest versus the South (OR 1.3, 95% CI 0.8-2.2). Steroid exposure was not associated with the occurrence of fractures (p=0.6).

Conclusions—Children with IBD are no more likely to have experienced a diagnosed fracture than age, sex, and gender-matched controls.

Keywords

Crohn's disease; ulcerative colitis; fracture; children

Background

Crohn's disease (CD) and ulcerative colitis (UC), collectively known as inflammatory bowel diseases (IBDs), are chronic, idiopathic conditions of the gastrointestinal tract that affect between 1 and 1.5 million Americans.[1-3] Nearly ¼ of cases have onset during the childhood or adolescent years. Both conditions are associated with high costs[4], substantial disease-specific morbidity, [5] and decreased quality of life[6, 7]. Additionally, patients often experience one or more nutritional complications including osteoporosis, growth failure, delayed puberty, anemia, and micronutrient deficiencies[8].

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A number of studies published over the last decade have described a high prevalence of osteopenia and osteoporosis in affected adult patients. A recent technical review published by the American Gastroenterological Association estimated the overall prevalence of osteoporosis to be 15% in the adult IBD population.[9] Furthermore several population based studies have shown that IBD is associated with an increased risk of fractures, particularly fragility fractures. A Danish study used hospital discharge data to determine the relative risk of fracture requiring hospitalization in 7072 patients with Crohn's disease and 8323 patients with ulcerative colitis compared to age and gender matched controls. This study found a mildly increased risk of fracture for CD [RR=1.19 (95% CI. 1.06-1.33)]. The association for UC was not statistically significant.[10] A major limitation to this study was reliance on hospital discharge data. Thus, outpatient fractures were not included. A second population based study in Manitoba, Canada used administrative data to compare the rates of both inpatient and outpatient fractures in IBD patients versus age, gender, and geographically matched controls. This study found a RR of 1.41 (95% CI 1.27-1.56) for IBD with no differences between CD and UC.[11] In the United States, a series of population-based studies in Olmsted county, MN, demonstrated a non-statistically significant increased risk of osteoporosis-related fractures (RR 1.4, 95% CI 0.7 to 2.7) but not total fractures in Crohn's disease patients.[12] Results showed a similar non-significant increased risk of osteoporotic fracture in UC patients compared to controls.[13] A final study using data from the General Practice Research Database in the UK also described a small excess risk of fractures in IBD patients, most prominent in the elderly.[14] Taken together, the results of epidemiological studies in adult populations suggest that patients with IBD have an increased risk of fracture, compared to the general population.

Whether children with IBD have an increased risk of fracture is largely unknown. Because the childhood and adolescent years are the time during which peak bone mass is attained, it is no surprise that decreased bone mass (a surrogate endpoint) has been reported in children with IBD.[15-18] However, the extent to which decreased bone mass leads to increased fractures (the clinical endpoint) remains unknown. Based on differences in bone physiology between children and adults, it is reasonable to suspect that effects of IBD on skeletal health may differ in children and adults.[19] Therefore, rigorous epidemiological studies of fracture risk in pediatric patients with IBD are needed.

In addition, the identification of modifiable risk factors for fracture is also necessary to inform screening and prevention guidelines. Such potential risk factors in the IBD population include corticosteroid treatment, which has been associated with diminished bone mineral density,[16, 20] and vitamin D deficiency.[21, 22]

The objectives of this study were 1) To determine whether children with IBD are at increased risk for fracture, compared to unaffected controls, and 2) To determine whether geographical region (a proxy for sun/vitamin D exposure) and oral corticosteroid use are associated with fractures among children with IBD.

Methods

Study Design and Data Source

We performed a cross-sectional study, analyzing the inpatient and outpatient insurance claims contained within the PharMetrics Patient-Centric Database (IMS Health, Watertown, MA) for the two year period January 1, 2003 through December 31, 2004. This longitudinal, patient-level database that pools together claims from 87 different health plans in 33 states has been reported to be representative of the national commercially-insured population on a variety of demographic measures, including geographic region, age, gender, and health plan

type[23] and has been used in previous epidemiological studies of inflammatory bowel disease. [3, 4]

Patient Selection

All individuals in the database less than 20 years of age with continuous health plan enrollment during the study period were eligible for inclusion in this analysis. We identified cases of CD and UC using a previously reported definition based on administrative data.[3] This definition included patients with at least 3 health care contacts, on different days, associated with an International Classification of Diseases, 9th Revision, Clinical Modification diagnosis code for CD (555.xx) or UC (556.xx), or patients with at least one claim for CD or UC and at least 1 pharmacy claim for any of the following medications: mesalamine, olsalazine, balsalazide, sulfasalazine, 6-mercaptopurine, azathioprine, infliximab, adalimumab, or enteral budesonide. For patients who had claims for both CD and UC, disease assignment was made according to the majority of the last 9 claims. For each case, we randomly selected up to 3 non-IBD controls from within the same health plan, matched on the basis of age (3 year increments), gender, and geographic region.

Identification of fractures

For both cases and controls, we identified claims for fractures occurring at each of the following sites using ICD-9 diagnosis codes: ankle, clavicle, foot, hand, humerus, femur, radius, skull, tibia, and vertebral. Prescriptions for oral corticosteroids (prednisone, prednisilone, methylprednisilone) were identified using National Drug Codes.

Statistical Analysis

We first determined the prevalence per 100,000 of fractures occurring at each site in the selected cases and controls. Similar analyses were performed for fractures occurring at any site and at multiple sites. Next, to compare the prevalence of fractures in IBD patients, relative to controls, we computed prevalence odds ratios using logistic regression. Each analysis was performed for IBD overall, and for CD and UC independently. Additionally, we performed a sub-analysis of the prevalence and odds ratios of fractures occurring at any site, after stratifying by age group (< 12 years, 12-17 years, and >17 years).

Among cases, we then compared the risk of fracture among patients residing in the South (expected low prevalence of vitamin D deficiency) to that in patients residing in the Northeast and Midwest (higher expected vitamin D deficiency) using logistic regression to control for corticosteroid exposure. Additionally, to compare the risk of fracture in cases versus controls residing in different regions, we also performed a sub-analysis of the prevalence and odds ratios of fractures occurring at any site, after stratifying by geographical region (Northeast/Midwest, South, West). Finally, we compared fracture risk by corticosteroid exposure using Student's t test and linear regression to control for geographical region.

All statistical analyses were performed using SAS version 9.2 (Cary, NC), and the study protocol was granted exemption from review by the Institutional Review Boards at the University of North Carolina at Chapel Hill because it involved the use of existing, de-identified data.

Results

Study Population

Our study population included 737 cases of pediatric Crohn's with 1,997 controls, and 488 cases of UC with 1,310 controls (Overall 1242 cases of IBD and 3353 controls).

Characteristics of included individuals are shown in Table 1. The mean age for both disease groups and controls was 15 years. Forty-four percent of CD patients and 47 % of UC patients were female. Each of the 4 major U.S. census regions was adequately represented.

Prevalence and risk of fractures

The prevalence per 100,000 population of fractures at any site and multiple fractures (different sites) for cases and controls are shown in Table 2. For CD and total IBD, there were no differences in the proportion of fractures occurring in cases versus controls (95% confidence intervals all cross 1). For UC, there was a nonsignificant trend towards increased fracture risk (OR 1.4, 95% CI 1.0-2.0) in cases. When analyzing the occurrence of multiple fractures (different sites) sites, there were no significant differences between cases of CD, UC, or total IBD versus their respective controls.

Fracture risks by site are displayed graphically in Figure 1. As illustrated, the confidence intervals for prevalence odds ratios for each site all crossed 1, indicating no significant differences between cases and controls. However, there was a strong trend towards increased risk of vertebral fractures (OR 2.7, 95% CI 0.8-10.8). For CD, the effect estimate was even higher (OR 5.4, 95% CI .05-60.0).

Table 3 illustrates the prevalence of 1 or more fractures in cases versus controls, stratified by age group. As expected, in the overall study population, the prevalence of fractures was higher in the youngest (pre-pubertal) age group, as compared to the middle (pubertal) and older (post-pubertal) age groups. Additionally, pre-pubertal children with IBD had a higher fracture risk than matched controls (OR 2.2, 95% CI 1.2-3.8). CD and UC-specific analyses stratified by age group were not possible due to sample size.

Among IBD patients, we next used geographical region as a surrogate indicator of vitamin D deficiency and assessed whether the risk of fracture was higher in residents in the Northeast/Midwest versus the South. We found an increased risk of fractures in the Northeast/Midwest, though this did not reach statistical significance (OR 1.3, 95% CO 0.8-2.2). After stratifying by region, the odds ratios for fracture in IBD patients versus controls in the Northeast/Midwest were slightly higher than in the south (1.1 versus 0.8), though the 95% confidence intervals were wide and overlapping (Table 3). The odds ratios for fracture were similar in the Northeast/Midwest and West. Finally, we compared the mean number of steroid prescriptions per year between those IBD patients who sustained fracture and those who did not. Patients with fractures had a mean of 1.6 (s.d. 3.5) prescriptions/year for oral steroids, as compared to a mean of 1.8 (s.d. 3.6) in patients without fracture ($p = 0.6$). After adjusting for geographical region, this comparison remained not statistically significant.

Discussion

In this large, epidemiological study of fracture risk in the pediatric IBD population, we found that children with IBD are no more likely to have experienced a fracture than age, sex, and gender-matched controls. However, we did observe a trend toward increased vertebral fractures, particularly in the CD population. We observed a higher prevalence of fractures among children less than 12 years of age, as compared to older children, a finding consistent with prior literature describing the age distribution of pediatric fractures [24, 25]. We also found that the fracture risk associated with IBD appeared to be age-specific. IBD children less than 12 years of age were at an increased risk of fracture when compared to non-IBD controls, however, no significant differences were observed in older children.

These findings extend the work of prior studies regarding fracture risk in both pediatric and adult populations in several ways. First, it comes as no surprise that fracture risk may differ

in the pediatric population, as compared with the adult population. In adults, bone mass is largely driven by the balance of bone resorption by osteoclast activity relative to bone formation by osteoblast activity. In children, however, bone mass is driven not only by this process of remodeling, but also by new bone formation which occurs through a combination of linear growth and bone modeling. Thus, one might expect the effects of IBD on skeletal health to be different in children and adults.[19] Furthermore, within the adult population, it appears that fracture risk is greatest in the elderly population,[14] further illustrating the concept that the effect of IBD on skeletal outcomes is an age-dependent process. Although no systematic studies of fracture risk in the pediatric population have been previosulsy published[19], the results of a recent retrospective study by Persad *et al* are consistent with the findings observed here. Persad *et al* surveyed parents of children with IBD to ascertain the prevalence of fractures in IBD patients, and unaffected siblings. Although limited by poor response rates and small sample size, this study also found no significant differences in fracture prevalence between IBD patients and their sibling controls.

Perhaps the most interesting finding in this current study was the trend toward increased vertebral fractures in IBD patients, and particularly those with Crohn's disease. Indeed, vertebral fractures are the most common form of osteoporosis-related fractures in the pediatric population, and have been reported in children with Crohn's disease.[26] Although the effect estimates were relatively strong (OR 2.7 for IBD overall, and 5.4 for CD), even the relatively large sample size of this study (1242 patients with IBD, 737 CD) did not provide adequate power to detect a significant association owing to the rarity of this outcome. Additionally, this study did not allow for the ascertainment of subclinical vertebral fractures, which are not uncommon in young adults with IBD[27].

A second notable finding in this study was the nonsignificant trend towards increased fracture prevalence in IBD patients from the Northeast and Midwest, as compared with the South. The risk of fracture in IBD patients versus controls followed a similar pattern. Although limited by the ecological nature of this analysis, we speculate that this may be a result of higher prevalence of vitamin D deficiency in northern latitudes[21]. Surprisingly, we did not find an association between corticosteroid use and fracture risk. This finding is consistent with a recent study using peripheral quantitative computed tomography to assess bone mass in an incident cohort of children with Crohn's disease. This study also found that glucocorticoids were not associated with decreases in bone mass.[18]

The strengths of this study are the large and diverse study population, including a wide range of health plans of varying size, type, and location. Thus, we believe this study population to be broadly generalizable to the U.S. commercially insured population. In addition, the identification of cases and controls from within a commercially insured population minimizes referral bias.

Several limitations must also be considered when interpreting the results of this study. First, the cross sectional study design limits the ability to make causal inferences. However, given that sustaining a fracture is unlikely to affect the risk of developing IBD (or need for corticosteroid treatment), we do not suspect a significant amount of temporal bias. Importantly, physical activity is not captured in administrative data. If children with IBD were less physically active than matched controls, then similar fracture rates would suggest that children with IBD fracture more easily. An additional limitation inherent to studies involving administrative data is the possibility of misclassification. We used a stringent case definition that required either multiple IBD-related health contacts or IBD-specific pharmaceutical claims to establish a diagnosis of CD or UC. This definition is similar to and represents a balance between administrative definitions that have been previously validated in the U.S. and Canada[28, 29]. Nevertheless, our study may not have identified milder cases

of IBD and/or fractures that did not seek medical attention or utilize health care services. The use of pharmacy claims to assess medication exposure has both advantages and disadvantages. Rather than relying on patient recall which may be inaccurate and/or medical records which indicate medications prescribed but not necessarily filled, outpatient pharmacy claims accurately reflect medications that were actually dispensed. However, such data do not capture adherence, another important indicator of exposure. Nevertheless, the use of pharmacy data as a measure of corticosteroid exposure has been used and accepted in many studies of IBD.[30, 31] Another limitation is that this study may not have been sufficiently powered to detect small to moderate differences in fracture risk between cases and controls, particularly in the CD and UC specific analyses. A final limitation is that the small number of Medicaid patients and lack of uninsured patients limits the generalizability of these results to such populations.

In conclusion, in this large epidemiological study, we found no significant differences in the risk of diagnosed fractures in pediatric IBD patients, as compared with age, gender, and region matched controls; however, a subanalysis in children less than age 12 demonstrated a significant positive association between IBD and fracture. These findings underscore the age-dependent effects of IBD on skeletal health outcomes. Importantly, this study does suggest the possibility of an increased risk of vertebral fractures, perhaps the most significant indicator of osteoporosis-related fracture in the pediatric age group.

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References

1. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology. 2004; 126:1504–17. [PubMed: 15168363]
2. Loftus EV Jr. The burden of inflammatory bowel disease in the United States: a moving target? Clin Gastroenterol Hepatol. 2007; 5:1383–4. [PubMed: 18054749]
3. Kappelman MD, Rifas-Shiman SL, Kleinman K, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. Clin Gastroenterol Hepatol. 2007; 5:1424–9. [PubMed: 17904915]
4. Kappelman MD, Rifas-Shiman SL, Porter CQ, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US children and adults. Gastroenterology. 2008; 135:1907–13. [PubMed: 18854185]
5. Witte J, Shivananda S, Lennard-Jones JE, et al. Disease outcome in inflammatory bowel disease: mortality, morbidity and therapeutic management of a 796-person inception cohort in the European Collaborative Study on Inflammatory Bowel Disease (EC-IBD). Scand J Gastroenterol. 2000; 35:1272–7. [PubMed: 11199366]
6. Cohen RD. The quality of life in patients with Crohn's disease. Aliment Pharmacol Ther. 2002; 16:1603–9. [PubMed: 12197839]
7. McLeod RS, Churchill DN, Lock AM, Vanderburgh S, Cohen Z. Quality of life of patients with ulcerative colitis preoperatively and postoperatively. Gastroenterology. 1991; 101:1307–13. [PubMed: 1936801]
8. Kappelman MD, Bousvaros A. Nutritional concerns in pediatric inflammatory bowel disease patients. Mol Nutr Food Res. 2008; 52:867–74. [PubMed: 18324705]
9. American Gastroenterological Association medical position statement: guidelines on osteoporosis in gastrointestinal diseases. Gastroenterology. 2003; 124:791–4. [PubMed: 12612916]

10. Vestergaard P, Mosekilde L. Fracture risk in patients with celiac Disease, Crohn's disease, and ulcerative colitis: a nationwide follow-up study of 16,416 patients in Denmark. Am J Epidemiol. 2002; 156:1–10. [PubMed: 12076883]
11. Bernstein CN, Blanchard JF, Leslie W, Wajda A, Yu BN. The incidence of fracture among patients with inflammatory bowel disease. A population-based cohort study. Ann Intern Med. 2000; 133:795–9. [PubMed: 11085842]
12. Loftus EV Jr, Crowson CS, Sandborn WJ, Tremaine WJ, O'Fallon WM, Melton LJ 3rd. Long-term fracture risk in patients with Crohn's disease: a population-based study in Olmsted County, Minnesota. Gastroenterology. 2002; 123:468–75. [PubMed: 12145800]
13. Loftus EV Jr, Achenbach SJ, Sandborn WJ, Tremaine WJ, Oberg AL, Melton LJ 3rd. Risk of fracture in ulcerative colitis: a population-based study from Olmsted County, Minnesota. Clin Gastroenterol Hepatol. 2003; 1:465–73. [PubMed: 15017646]
14. Card T, West J, Hubbard R, Logan RF. Hip fractures in patients with inflammatory bowel disease and their relationship to corticosteroid use: a population based cohort study. Gut. 2004; 53:251–5. [PubMed: 14724159]
15. Sylvester FA, Wyzga N, Hyams JS, et al. Natural history of bone metabolism and bone mineral density in children with inflammatory bowel disease. Inflamm Bowel Dis. 2007; 13:42–50. [PubMed: 17206638]
16. Boot AM, Bouquet J, Krenning EP, de Muinck Keizer-Schrama SM. Bone mineral density and nutritional status in children with chronic inflammatory bowel disease. Gut. 1998; 42:188–94. [PubMed: 9536942]
17. Gokhale R, Favus MJ, Karrison T, Sutton MM, Rich B, Kirschner BS. Bone mineral density assessment in children with inflammatory bowel disease. Gastroenterology. 1998; 114:902–11. [PubMed: 9558278]
18. Dubner SE, Shults J, Baldassano RN, et al. Longitudinal assessment of bone density and structure in an incident cohort of children with Crohn's disease. Gastroenterology. 2009; 136:123–30. [PubMed: 19026647]
19. Sylvester FA. Do bones crack under the effects of inflammatory bowel disease in children? J Pediatr Gastroenterol Nutr. 2006; 43:563–5. [PubMed: 17130728]
20. Bourges O, Dorgeret S, Alberti C, Hugot JP, Sebag G, Cezard JP. Low bone mineral density in children with Crohn's disease. Arch Pediatr. 2004; 11:800–6. [PubMed: 15234375]
21. Pappa HM, Gordon CM, Saslowsky TM, et al. Vitamin D status in children and young adults with inflammatory bowel disease. Pediatrics. 2006; 118:1950–61. [PubMed: 17079566]
22. Pappa HM, Grand RJ, Gordon CM. Report on the vitamin D status of adult and pediatric patients with inflammatory bowel disease and its significance for bone health and disease. Inflamm Bowel Dis. 2006; 12:1162–74. [PubMed: 17119391]
23. Stempel DA, Mauskopf J, McLaughlin T, Yazdani C, Stanford RH. Comparison of asthma costs in patients starting fluticasone propionate compared to patients starting montelukast. Respir Med. 2001; 95:227–34. [PubMed: 11266241]
24. Landin LA. Fracture patterns in children. Analysis of 8,682 fractures with special reference to incidence, etiology and secular changes in a Swedish urban population 1950-1979. Acta Orthop Scand Suppl. 1983; 202:1–109. [PubMed: 6574687]
25. Khosla S, Melton LJ 3rd, Dekutoski MB, Achenbach SJ, Oberg AL, Riggs BL. Incidence of childhood distal forearm fractures over 30 years: a population-based study. JAMA. 2003; 290:1479–85. [PubMed: 13129988]
26. Semeao EJ, Stallings VA, Peck SN, Piccoli DA. Vertebral compression fractures in pediatric patients with Crohn's disease. Gastroenterology. 1997; 112:1710–3. [PubMed: 9136852]
27. Klaus J, Armbrecht G, Steinkamp M, et al. High prevalence of osteoporotic vertebral fractures in patients with Crohn's disease. Gut. 2002; 51:654–8. [PubMed: 12377802]
28. Herrinton LJ, Liu L, Lafata JE, et al. Estimation of the period prevalence of inflammatory bowel disease among nine health plans using computerized diagnoses and outpatient pharmacy dispensings. Inflamm Bowel Dis. 2007; 13:451–61. [PubMed: 17219403]
29. Bernstein CN, Blanchard JF. The epidemiology of Crohn's disease. Gastroenterology. 1999; 116:1503–4. [PubMed: 10391739]

30. Herrinton LJ, Liu L, Fireman B, et al. Time trends in therapies and outcomes for adult inflammatory bowel disease, Northern California, 1998-2005. Gastroenterology. 2009; 137:502–11. [PubMed: 19445944]

31. Lewis JD, Aberra FN, Lichtenstein GR, Bilker WB, Brensinger C, Strom BL. Seasonal variation in flares of inflammatory bowel disease. Gastroenterology. 2004; 126:665–73. [PubMed: 14988820]

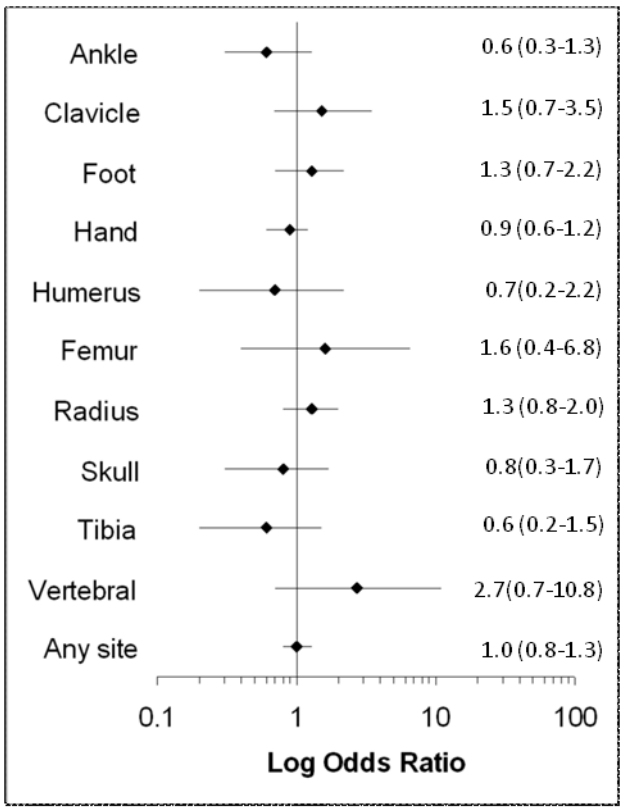

Figure 1.
Fracture Risk by Site in U.S. Children with IBD. Forest plots depict the prevalence odds ratios and 95% confidence intervals for fractures occurring at various anatomic sites, as well as at any site.

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Table 1

Patient and Control Demographics

	Crohn's disease		Ulcerative Colitis		Total IBD	
	Cases	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**
n	737	1997	488	1310	1242	3353
Mean age (s.d.)	15 (3.2)	15 (3.4)	15 (3.7)	15 (3.7)	15 (3.4)	15 (3.5)
Sex						
% Female	44	44	47	48	45	46
Region						
% Northeast	28	27	26	24	27	26
% Midwest	23	24	26	28	25	26
% West	28	29	26	26	27	28
% South	20	20	22	22	21	20

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Table 2

Prevalence and risk of fractures among U.S. children with IBD

	Crohn's disease		Ulcerative Colitis		Total IBD	
	Cases n=737	Controls n=1997	Cases n=488	Controls n=1310	Cases n=1242	Controls n=3353
Any Fracture						
# events	60	200	47	91	110	294
Prevalence per 100,000	8,141	10,015	9,631	6,947	8,857	8,769
Odds ratio (95% CI)	0.8 (0.6-1.1)		1.4 (1.0-2.0)		1.0 (0.8-1.3)	
Multiple Fractures						
# events	11	35	3	19	15	55
Prevalence per 100,000	1,493	1,753	615	1,450	1,208	1,640
Odds ratio (95% CI)	0.8 (0.4-1.7)		0.4 (0.1-1.4)		0.7 (0.4-1.3)	

Table 3

Prevalence and risk of sustaining 1 or more fractures among U.S. children with IBD, stratified by age and geographical region

	IBD Cases	Controls
Age 0-11		
n	186	515
# Events	22	32
Prevalence per 100,000	11,828	5,850
Odds ratio (95% CI)	2.2 (1.2-3.8)	
Age 12-17		
n	725	1938
# Events	69	206
Prevalence per 100,000	9,517	10,630
Odds ratio (95% CI)	0.9 (0.7-1.2)	
Age 18-20		
n	331	868
# Events	19	56
Prevalence per 100,000	5,740	6,452
Odds ratio (95% CI)	0.9 (0.5-1.5)	
Northeast/Midwest		
n	648	1754
# Events	62	150
Prevalence per 100,000	9,568	8,552
Odds ratio (95% CI)	1.1 (8.8-1.5)	
South		
n	337	923
# Events	24	84
Prevalence per 100,000	7,122	9,101
Odds ratio (95% CI)	0.8 (0.5-1.2)	
West		
n	257	676
# Events	24	60
Prevalence per 100,000	9,339	8,876
Odds ratio (95% CI)	1.1 (0.6-1.7)	